REMARKS

This amendment is made to correct typographical errors, to resolve any confusion as to what the Applicants deem is their invention and to put the claims in condition for allowance. Support for the amendments can be found throughout the specification as filed. No new matter is introduced by this amendment.

The Invention.

The present invention provides a novel endoglucanase nucleic acid sequence, designated *egl6*, and the corresponding EGVI amino acid sequence. The invention also provides expression vectors and host cells comprising a nucleic acid sequence encoding EGVI, recombinant EGVI proteins and methods for producing the same.

Status of the Application.

Claims 1-17, 19-20, 22-24, and 26 are pending in the application. Claims 1, 18, 21, 25 and 27-36 have been cancelled herein without prejudice. Applicants retain the right to file further continuation and divisional applications on any non-elected claim and on the subject matter of any claim previously or presently canceled.

Claims 2, 4 and 26 have been amended herein to clarify what Applicants consider the subject matter of the invention. No new matter is introduced by these amendments.

Applicants have recognized the need for an updated Sequence Listing and will provide one shortly.

Specification.

The disclosure was objected to as containing an embedded hyperlink and/or other form of browser-executable code. Applicants have amended the specification to remove the hyperlinks. Withdrawal of the objection is respectfully requested.

35 U.S.C. §112, first paragraph.

Claims 1-17, 19-20, 22 and 26

Claims 1-17, 19-20, 22 and 26 stand rejected under 35 USC §112, first paragraph as failing to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. Specifically, the Examiner asserts that the claims are so broad because they encompass any variant or mutant

polynucleotide encoding polypeptides that have 85%, 90% or 95% sequence identity to SEQ ID NO:5 (as noted above Applicants will provide a new sequence listing shortly) and that it would require undue experimentation to identify regions that could be changed. Applicants respectfully traverse.

First, Claim 1 has been cancelled without prejudice. Second, Claim 2 has been amended to recite 90%, 95% or 98% sequence identity to SEQ ID NO:5 or 95% sequence identity to SEQ ID NO:2. Applicants believe that a person skilled in the art would not require undue experimentation to arrive at the claimed polynucleotides as claim 2 is now limited to Family 74 glycosyl hydrolases.

It is well settled law that the specification does not need to teach that which is well known in the art. Glycosyl hydrolases, including those in Family 74, are well characterized. As noted in the specification at page 24, the BLAST search performed by the Applicants indicated that the proteins with the highest identity are from glycosyl hydrolase Family 74.

One skilled in the art recognizes that classification of glycoside hydrolases into families is based on amino acid sequence similarities. Because there is a direct relationship between the amino acid sequence of a protein and its folding similarities, such a classification is expected to reflect the structural features of these enzymes better than their substrate specificity. Such a classification system can help to reveal the evolutionary relationships between these enzymes and provide a convenient tool to derive mechanistic information (http://afmb.cnrs-mrs.fr/CAZY/index.html). Some members of the Family 74 glycosyl hydrolase include Aspergillus aculeatus avicelase III (SwissProt O74170), Aspergillus niger endoglucanase C (GenPept AAK77227.1), and Thermotoga maritima Cel74 (SwissProt Q9WYE1). Conserved residues are known for this family as well which will aid the skilled practioner in aligning sequences. Thus, this provides information on the various regions of the enzyme, and allows alignment and characterization of the identity of other proteins with the currently claimed EG VI, and was known to the skilled artisan at the time of filing.

The Examiner asserts that the art is unpredictable. Applicants respectfully disagree. As a point of reference, Applicants direct the Examiner's attention to Mosimann *et al.*, PROTEINS: Structure, Function and Genetics, vol. 23, pp. 301-317 (1995) (first page submitted herewith), wherein the author indicates that where sequence identity between the target and the template is greater than 70%, comparative molecular modeling is highly successful. (See attached abstract).

The Examiner further asserts that it is not routine to in the art to screen for multiple modifications. Applicants have provided guidance on applicable assays for measuring endoglucanase activity. Thus, one skilled in the art would be able to quickly determine if the protein possesses the required activity. As for the the number of changes, using any of the well known techniques in the art (e.g., MALDI-TOF) one can routinely sequence a protein, even large proteins, with ease. Once again, Applicants are not required to teach that which is well known in the art.

Withdrawal is respectfully requested.

Claims 1-17, 19-20, 22 and 26

Claims 1-17, 19-20, 22 and 26 stand rejected under 35 USC §112, first paragraph as allegedly containing subject which was not described in the specification in such a way as to convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicants respectfully traverse.

Applicants have cancelled claim 1 rendering the rejection moot for that claim. As the rejection relates to the other claims Applicant notes that the claims are direct to a specific set of naturally occurring enzymes with endoglucanase activity.

As noted above it is not necessary to teach that which is well known in the art. Persons skilled in the art are aware of the codons that encode the various amino acids. With the information on tertiary structure for Family 74 glycosyl hydrolases and the primary structure of EG VI a person skilled in the art would be able to appreciate the Applicants could have had the claimed invention at the time the instant application was filed. Applicants note that it is not necessary under §112 that every claimed embodiment be specifically exemplified. Applicants respectfully submit that a skilled artisan would be able to glean from the specification the metes and bounds of the invention. Applicants also note that the number of polypeptides encoded by the polynucleotides encompassed by the present claims is finite and well within the skill of the ordinary artisan.

Withdrawal is respectfully requested.

35 U.S.C. §102.

Claims 1-12, 14-15, 17 and 19-20 stand rejected under 35 USC §102(b) as being anticipated by Shin *et al.* (Sanop Misaengmul Hakhoechi, (Korean J. Appl. Microbiol. Biotechnol.) 1998, 26(5):406-412). Applicants respectfully traverse.

Shin *et al.*, fails to provide a nucleotide sequence that would allow comparison with the Applicants described *egl6* nucleotide. Furthermore, an examination of the information on the protein expressed by Shin *et al.* reveals that the protein has a molecular weight of approximately 66kD. The EG VI described in the instant application has a molecular weight of approximately 87kD.

Furthermore, the EG VI of Shin was isolated from a *Trichoderma* sp C-4, not from *Trichoderma reesei*. From the DNA sequence of *Trichoderma* sp. C-4 egl6, the ORF consists of 1254 bp and encodes an expected 417 AA (ca. 46 kDa) polypeptide. See Page 410, second col, first paragraph. This is in contrast to the presently described invention which has predicted molecular weight of 87.1kDa and is over 800 amino acids in length. See Page 24 and Figure 2 of the specification.

A reference that merely contains substantially the same elements or only broadly teaches the invention is insufficient to establish anticipation. *Jamesbury Corp. v. Litton Industrial Products, Inc.*, 756 F.2d 1556, 1560, 225 USPQ 253, 256 (Fed. Cir. 1985); *Kalman v. Kimberly-Clark Corp.*, 713 F.2d 760, 772, 218 USPQ 781, 789 (Fed. Cir. 1983). Shin *et al.* teaches an endoglucanase encoded by a gene termed *egl6* but it is clear from the SDS-PAGE gel that the Shin el al. expression product is not the same as Applicants. Moreover, there is no nucleic acid sequence given. Thus, Shin *et al.* fails to anticipate the current invention.

Withdrawal of the rejection is respectfully requested.

35 U.S.C. §103.

The Examiner has maintained the rejection of Claim 26 as allegedly obvious over the combination of Shin, *et al.* in view of Ward, *et al.* (US Pat. No. 6,265,204; the '204 patent). Applicants respectfully traverse the rejection.

Claim 26 is currently directed to the expression of EG VI as a chimeric protein in an *Aspergillus* host cell. The inventive endoglucanase is expressed with signal sequence heterologous to the endoglucanase, thus producing the chimeric protein.

A *prima facie* case of obviousness requires the Examiner to cite to a combination of references which (a) suggests or motivates one of skill in the art to modify their teachings to yield the claimed invention, (b) discloses the elements of the claimed invention, **and** (c) provides a reasonable expectation of success should the claimed invention be carried out. Failure to establish **any** one of these requirements precludes a finding of a *prima facie* case of

obviousness and, without more, entitles Applicants to withdrawal of the rejection of the claims in issue.[1] Applicants assert that the Examiner has failed to establish not one, but all three requirements as discussed below.

A. Shin *et al.* fails to suggest or motivate one of skill in the art to modify their teachings to yield the claimed invention

Shin, *et al.* is directed to the expression of an endoglucanase in *S. cerevisiae*, a yeast. *S. cerevisiae* is an excellent host for heterologous protein production, since it can be grown to high cell densities on simple media and many proteins can be correctly folded and secreted to the culture medium. The eukaryotic nature and GRAS status have made *Saccharomyces cerevisiae* a popular host for the industrial production of heterologous proteins. In addition, Shin *et al.* shows that the majority (i.e., approximately 80%) of the enzyme produced by the yeast is secreted. See Figure 3. Thus, there would be no motivation for the skilled artisan to use another expression system such as that described in the '204 patent.

B. The combination of Shin *et al.* and the '204 patent does not disclose the elements of the claimed invention

Shin *et al.* uses the yeast *adh1* promoter to achieve production in *S. cerevisae*. There is no teaching that this promoter would work in the filamentous fungi, i.e., *Aspergillus*, of the '204 patent. There is also no teaching that a signal sequence heterologous to the endoglucanase is necessary or desirable. Nor, as described above, is there a teaching that you would want to move to another expression system.

The '204 patent is directed to an expression system that comprises "two coding nucleic acids each of which encode desired polypeptides." In the presently claimed invention does not require two or more copies the desired polypeptide, i.e., EG VI.

The selection of the combination suggested by the Examiner is not fairly suggested in the prior art. The Examiner impermissibly picks and chooses ingredients without considering the invention as a whole, and looks suspiciously like hindsight reconstruction reached through the teachings of Applicants' disclosure. At best, the analysis is obvious to try.

C. The combination of Shin *et al.* and the '204 patent does not provide a reasonable expectation of success should the claimed invention be carried out

Under patent law with regard to obviousness, a reasonable expectation of success is to be assessed from the perspective of one of ordinary skill in the art at the time the invention was made. At the time the invention was made it was well established that not only were there

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[1] *See e.g., Northern Telecom Inc. v. Datapoint Corp.*, 15 USPQ2d 1321, 1323 (Fed. Cir. 1990); and *In re Dow Chemical Co.*, 837 F.2d 469, 5 USPQ2d 1529 (Fed. Cir. 1988).

differences in the expression and secretion levels of various constructs within a single host organism but also that similar constructs give different results in different organisms. See Ward *et al* (Biotechnology (1990) 8:435-440) page 435, last full paragraph; copy of page 435 attached. *This supports Applicants' position that one skilled in the art would not have a reasonable expectation of success in transferring one expression construct from one host system to another OR that alterations in an expression construct, e.g., using a truncated gene instead of a full-length gene, would work.*

Withdrawal of the rejection is respectfully requested.

CONCLUSION

In light of the above amendments, as well as the remarks, the Applicants believe the pending claims are in condition for allowance and issuance of a formal Notice of Allowance at an early date is respectfully requested. If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (650) 846-7615.

Respectfully submitted,
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